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Effectiveness of Laser Acupoints on Women With Polycystic Ovarian Syndrome: A Randomized Controlled Trial

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Abstract

Introduction: Polycystic ovarian syndrome (PCOS) is one of the most widely recognized reasons for infertility. The aim of this study was to examine the impact of laser acupuncture on PCOS women.

Methods: Twenty-five PCOS women were randomly allocated to either the study group (SG; n=13), treated by laser acupuncture, or the control group (CG; n = 12). Blood hormonal levels and insulin resistance were measured at baseline and after 12 weeks of intervention.

Results: The pre-intervention levels showed no statistically significant differences between SG and CG for baseline characteristics ($P>0.05$). After 12 weeks of intervention, within-group analyses showed that body mass index (BMI), blood hormonal levels, and insulin resistance were significantly decreased ($P<0.05$), while no significant changes in follicle-stimulating hormone ($P>0.05$) were recorded in the 2 groups. Between-groups analyses showed that most outcomes measures were significantly decreased ($P<0.05$) in SG compared with CG, with no significant changes in FSH and BMI ($P>0.05$).

Conclusion: Laser acupuncture can be suggested as an effective management for PCOS women.

Keywords: Polycystic ovary syndrome; Blood hormonal levels; Insulin resistance; Laser; Acupuncture.

Introduction

Polycystic ovarian syndrome (PCOS), is the most recognized endocrine dysfunction affecting 5 to 10% women of reproductive age.[1] While about 21% of women have PCOS,[2] it impacts 15%-20% of infertile women.[3]

Insulin resistance (IR) is the most well-known characteristics of PCOS, represented in 85% of these women.[4] An additional basic aspect of PCOS, high androgen levels, influences about 60% to 80% of PCOS women and is able to produce medical signs such as hirsutism, acne, and alopecia.[5]

The National Institutes of Health (NIH) suggested investigative criteria for PCOS requiring the concurrent existence of androgen excess (biochemical and/or clinical) and ovarian disorder.[6] In 2003, the Rotterdam criteria define PCOS as the presence of at least 2 criteria from androgen excess, ovulatory disorder and polycystic ovarian morphology.[7] The Androgen Excess Society (AES) reviewed PCOS investigative criteria that need to exits as androgen excess and menstrual disorder and/or PCO morphology.[8]

However, the actual incidence of PCOS in the society is the theme of a persisting discussion due to the specific sampling methodology used in each of the different studies plus study design limitations. Nevertheless, PCOS incidence based on the NIH criteria is appraised to be about 6% to 8%,[9] with the application of the Rotterdam criteria, the incidence increased to 15% to 25%,[10] while the implementation of the Androgen, AES recommendations puts PCOS incidence at about 10 to 15%.[9]

PCOS is a complex of symptoms of unknown cause and is defined as a heterogeneous dysfunction that results in Hyperandrogenism, existing evidence suggests that the ovarian theca cells are the real wellspring of the androgen generation and emission which assume a key part in the PCOS etiology.[11]

In addition, the hypothalamic-pituitary-ovarian (HPO) axis and IR may cause the PCOS. Changes in the sympathetic nervous system activity have also been proposed in the list of causes of this syndrome.[12]

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PCOS is related to the progress of severe endocrine, metabolic, cardiovascular, reproductive, and psychological problems.[2]

Due to its heterogeneous nature, an effective treatment of PCOS requires a consistent, multi-axes strategy with interdisciplinary experience, established on a strong evidence base to guide the unification of care. Many women with PCOS require long-lasting treatment that extends from lifestyle interference to precise medical or surgical methods. Medical treatments are effective although have several complications. Oral contraceptives are used as the first-line of treatment in PCOS, they minimize hirsutism and acne but have many negative effects on glucose tolerance, coagulability and fertility.[13]

Acupuncture, a treatment that goes back 3000–5000 years of clinical practice, is a basic part of traditional Chinese medication and has turned out to be perceived in Western medicine more as a supplement or other choice to traditional treatments. Acupuncture therapy in female with PCOS and ovulatory disorder has been known to bring enduring useful results on the endocrine system and menstrual cycle, without complications.[14]

Laser acupuncture is considered to be an effective alternative to conventional needle acupuncture, is valuable in patients who are needle fearful, or can be used as a safe (e.g., virus C infection), non-invasive technique of treatment and a suitable method for stimulation of difficult points in the region of perineum or genitals.[15] To our knowledge, no trial study has been done to address the therapeutic effect of laser acupoints on women with reproductive disorders. For that reason, the purpose of the present study is to assess the outcome of laser acupoints on female with PCOS.

Methods

Participants

Twenty-nine female with PCOS (n = 29) aged between 19 and 23 years were recruited to the study in the gynecology department of the Kafrelsheikh General Hospital, Kafrelsheikh, Egypt. The evaluation procedures were explained to each participant. Prior to baseline measurements, 4 women dropped out, 2 because they wished to withdraw from the study and 2 were relocating to another city. Of the remaining women, 25 were haphazardly recruited for blood examinations.

Assessments were done at (1) baseline and (2) after 12 weeks of intervention, from April to December 2016.

Inclusion and Exclusion Criteria

The inclusion criteria were participants aged between 19 and 23 years, body mass index (BMI) not exceeding 30 kg/m^2. PCOS women were assignable for randomization if they had clinical and/or biochemical signs of androgen excess (hirsutism or acne), together with one of the next symptoms: oligomenorrhea or amenorrhea (oligomenorrhea is generally defined as a cycle duration of more than 35 days while in amenorrhea the inter-cycle period exceeds 90 days), screened polycystic ovaries (≥12 follicles with a 2-9 mm diameter on the ovary and/or ovarian volume >10 cm^3) disclosed by ultrasonography in one or both ovaries, according to the AES.[8]

Exclusion criteria were: recognized endocrine causes of hyperandrogenemia, androgen-secreting neoplasm, Cushing syndrome, acromegaly, hyperprolactinemia, thyroid dysfunction, hypothalamic amenorrhea, ovarian insufficiency, congenital adrenal or ovarian hyperplasia and a drug-related condition.

Each woman was excluded from the study if she missed 3 sessions.

Design

This is a randomized controlled trial with blinding of participants and examiners. As participants were blinded to the knowledge of the group they would create, since the participant selected a numbered envelope, which did not let the participant to know the group that she would comprise (study or control). Thus, the PCOS participants were randomized into blocks and allocated, using a simple, non-probability sampling method, to either the study group (SG; n = 13), treated by laser acupoints or the control group (CG; n = 12), which were treated by placebo laser acupoints.

Sample-Size Calculation

Assuming a 30% improvement in blood hormonal levels of PCOS women in the study group, based on a sample with the power size estimation of the study beta of 80%, and to detect the effect size of difference 5%, with a significance level of $P < 0.05$, 10 participants were required.

Intervention

The condition of PCOS women randomized to the group treated by laser acupoints for 3 months was assessed at baseline and after 12 weeks (end of intervention), during which time they undertook two sessions per week during first 2 weeks, one session/week through 4 weeks, and one session every seconds week for 6 weeks, in a total of 11 sessions through 12 weeks.[16]

Acupoints selection was based on previous studies[14] and clinical trials treating PCOS women.

Laser acupoints were selected according to innervations of the ovaries (Th_{12}–L_2, S_2–S_4) to modulate HPO and the hypothalamic-pituitary-adrenal (HPA) axes to support hormonal balance[17] (Table 1).

An infrared laser (Acu-Lase, Petrolaser, Russia) with 830 nm wavelength, 10 mW power output and 0.5 J energy was applied 60 seconds for each acupoint. The head of the machine was used perpendicularly, with direct contact to each point.

The physiotherapist responsible for performing laser acupoints had experience in acupuncture within women's health. All participants in the intervention group were

Table 1. Laser Acupoints With Anatomical Position and Innervation

Point	Location	Innervation
Ren4 (Unilateral)	On the midline, 3 cun lower to the umbilicus.	Anterior cutaneous nerve of the subcostal nerve
Ren5 (Unilateral	On the midline, 2 cun lower to the umbilicus.	Anterior cutaneous branch of the 11th intercostal nerve
St29 (Bilateral)	4 cun under the umbilicus, 2 cun sideways to the midline.	The iliohypogastric nerve (Th_{6-12}).
Sp6 (Bilateral)	3 cun higher than the tip of the medial malleolus on the posterior margin of the tibia.	Superficially, the medial crural cutaneous nerve; deeper, in the posterior aspect, the tibial nerve (L_{4-5}, S_{1-2}).

Cun is the estimation of one "body inch" utilized to find acupuncture points. Estimation is constantly taken from the patient's hand. The breadth of the thumb is 1 cun, breadth of 2 fingers is 1.5 cun, 4 fingers are 3 cun.

given an info brochure, that included advice on a healthy diet as a low-carbohydrate and high-protein diet,[18] high dietary fiber, and less saturated fat,[19] were instructed to engage in aerobic exercise, fast walking for at least 30 - 45 min, 3 days a week.[16] Women in the control group were treated by placebo laser acupoints with the same pieces of advice on healthy diet and exercise as in the intervention group.

Neither group was undergoing physiotherapy or any other treatment during the intervention period.

Outcome Measures

The whole analyses were performed at a certified laboratory at the Department of Clinical Chemistry, Kafrelsheikh General Hospital. Blood tests included serum free testosterone (FT), serum total testosterone (TT), luteinizing hormone (LH) and follicle-stimulating hormone (FSH), LH/FSH ratio**,** anti-Müllerian hormone (AMH) and insulin sensitivity was calculated with a homeostasis model assessment of insulin resistance (HOMA-IR).[20] Blood samples were taken independently on day 2 or 3 of the follicular phase of the menstrual cycle because the majority of the participants had ovarian dysfunction.

All the biochemical checkups were done for both groups (SG and CG) at (1) baseline and (2) after 12 weeks of intervention**.**

Data Analysis

The collected data were categorized, tabulated and analyzed using descriptive statistics in terms of mean ± standard deviation, frequency, and percentage. The paired *t* test was used to analyze and compare blood hormonal levels within each group (SG or CG) before and after the intervention. The independent *t* test was carried out to evaluate differences between both groups (SG and CG) before and after the intervention. A *P* value <0.05 was considered statistically significant. Data analysis was done using SPSS software version 16.

Results

Out of the 34 women originally contacted at their first visit, 29 achieved the inclusion criteria. Of these, 4 withdrew from the study and 25 PCOS women (aged 20 ± 1.2 years) were randomly allocated into the study group (SG; n = 13) or a control group (CG; n = 12) (Figure 1).

PCOS phenotype according to AES[8] was as follows: in the study group, 6 (46.1%) had androgen excess and ovulatory dysfunction, 4 (30.8%) had androgen excess and PCO morphology, and 3 (23.1%) had androgen excess, ovulatory dysfunction, and PCO morphology; in the control group, 5 (41.7%) had androgen excess and ovulatory dysfunction, 5 (41.7%) had androgen excess and PCO morphology, and 2 (16.6%) had androgen excess, ovulatory dysfunction, and PCO morphology.

Baseline characteristics of the participants are summarized in Table 2. There were no statistically significant differences between both groups (SG and CG) in any of these characteristics ($P > 0.05$).

The mean application of laser acupoints sessions in the study group was 10 ± 0.1 out of 11 possible sessions. Ten out of the 13 women in the study group (76.9 %) performed at least 9 (81.8%) of weekly sessions. No hazards were reported by the participants.

Within-group analyses revealed that BMI, blood hormonal levels, and IR were significantly decreased ($P < 0.05$), with no significant change in FSH ($P > 0.05$) in the 2 groups (Tables 3 and 4) (Figures 2 and 3).

Between-group analyses at the end of intervention revealed that most outcomes measures were significantly decreased ($P < 0.05$) in SG contrasted with CG, with no significant changes in FSH and BMI ($P > 0.05$) between the two groups (Table 5) (Figure 4).

Menstrual and ovulation frequencies were as follows: in the study group, 9 of 13 (69.23 %) were oligo-or amenorrhoeic before the intervention and 6 (66.7 %) reported 3 regular menses throughout the study: in the control group, 7 of 12 (58.33 %) were oligo-or amenorrhoeic before the intervention and 5 (41.67 %) reported 3 regular menses throughout the study.

Discussion

The purpose of our study was to investigate the impact of treatment with laser acupoints on PCOS women. The progress in the different outcomes was evaluated by comparing the post-treatment results with those at the pretreatment, evaluating improvement within group separately. In addition, we compared the results between both groups.

This study showed that, within groups, we have found an enhancement in all measures at the end of the intervention, with no significant variation within the two

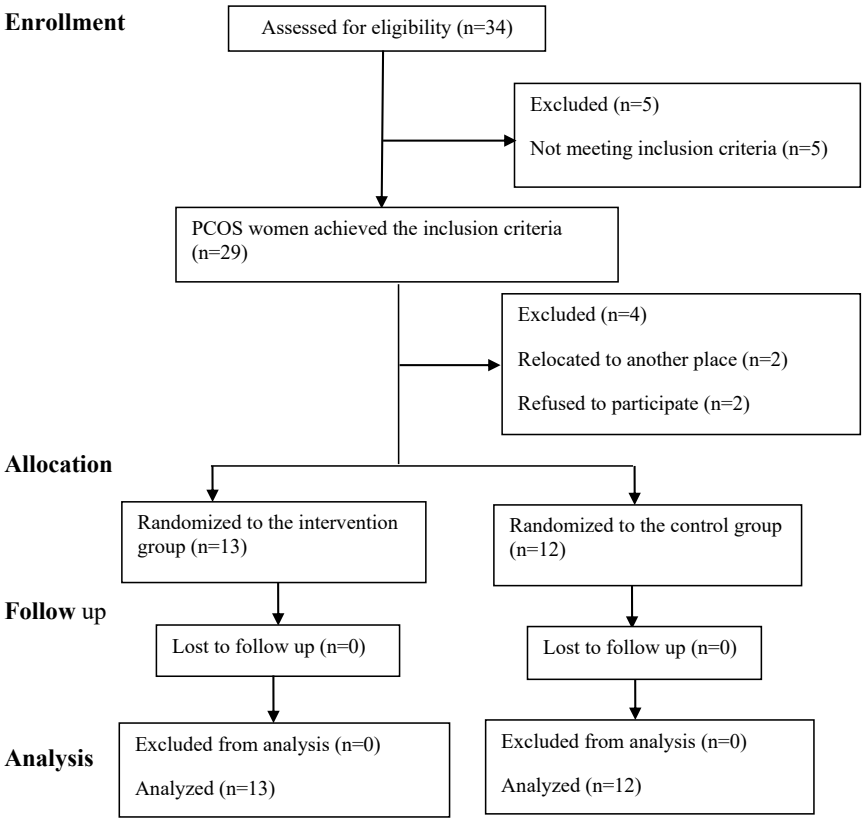

Figure 1. Flowchart of the Participants During the Study.

groups regarding the FSH level.

PCOS women demonstrate a state of IR and hyperinsulinemia, thus, androgen generation can be overstimulated. This is mainly obvious in the existence of increased BMI.[21] Hyperinsulinemia contributes to the unusual gonadotropin-releasing hormone (GnRH) secretion, in spite of the fact that the mechanism is not clear.[22]

An increase in serum LH levels is conflictingly found in PCOS women, due to a GnRH increase in the sufficiency and recurrence of pulsatile LH secretory pattern.[23] Levels of FSH in PCOS appear to be within the lower follicular range, and response to GnRH is relatively similar to ovulatory controls.[24] All these factors increase the LH/FSH ratio; the most obvious neuroendocrine characteristic regulating abnormal ovarian follicle maturity in PCOS is increased LH pulsatility regarding both frequency and amplitude, with relatively low FSH secretion.[25] On account of an increased LH/ FSH ratio, the ovarian granulosa cells cannot aromatize the androgens to estrogens, which leads to diminished estrogen levels and ensuing anovulation[26] that are consistent with our results.

Table 2. Baseline Characteristics of PCOS Women in the 2 groups

Variables	Mean ± SD of Baseline Characteristics of Participants		*P* Value
	Study Group (n=11)	Control Group (n=10)	
Age (y)	20.2±0.3	19.8±0.8	0.52
BMI(kg/m²)	27.15±2.1	26.9±1.7	0.61
FT, ng/dL	2.1±0.1	1.9 ±0.3	0.19
TT, ng/dL	69.5±2.1	66.3±1.3	0.20
LH, mIU/mL	10.1±1.3	11.3±0.3	0.63
FSH, mIU/mL	4.9±0.8	5.0±0.2	0.70
LH/FSH ratio	2.4±0.3	2.5±0.5	0.81
AMH, ng/mL	12.0±1.9	13.3±1.4	0.31
HOMA-IR	2.9±1.3	2.5±1.4	0.21

HOMA-IR, the indicator of which was considered according to the rule: [fasting plasma glucose (mg/dL) × fasting plasma insulin concentration (mU/L)]/405.

AMH levels in PCOS women emphatically correspond with antral follicle number and androgen levels, are increased 2-3 fold,[27] and are lessened in parallel with a decrease of androgen level in our study.

The most excellent therapeutic approach for weight reduction in obese PCOS women has not yet been explored. Lifestyle changes, mainly a caloric restriction diet alone or with exercises,[28] are suggested as a first-line of treatment in the overweight and obese PCOS women.[29] Dietetic-induced weight reduction enhances IR and hyperinsulinemia. Both fasting and glucose-stimulated insulin are predisposed to significantly diminish after a weight reduction by about 5%–10%.[28]

Table 3. Comparison of the Mean of Outcomes Measures Within Study Group After 12 Weeks of Intervention

Variables	Mean ± SD Outcomes Measures Study Group (n=11)		*P* Value
	Baseline	End of Intervention	
BMI (kg/m²)	27.15±2.1	25.6±0.1	0.04
FF, ng/dL	2.1±0.1	1.09±0.1	0.02
TT, ng/dL	69.5±2.1	60.0±0.1	0.04
LH, mIU/mL	10.1±1.3	6.9±0.9	0.01
FSH, mIU/mL	4.9±0.8	4.8±0.6	0.52
LH/FSH ratio	2.4±0.3	1.3±0.0	0.02
AMH, ng/mL	12.0±1.9	8.5±1.3	0.01
HOMA-IR	2.9±1.3	1.9±1.5	0.01

Table 4. Comparison of the Mean of Outcomes Measures Within Control Group After 12 Weeks of Intervention

Variables	Mean ± SD Outcomes Measures Control Group (n=10)		*P* Value
	Baseline	End of Intervention	
BMI (kg/m²)	26.9 ±1.7	25.0 ±1.2	0.04
FF, ng/dL	1.9 ±0.3	1.5±0.05	0.01
TT, ng/dL	66.3±1.3	63.0±1.9	0.05
LH, mIU/mL	11.3±0.3	9.9±0.2	0.02
FSH, mIU/mL	5.0±0.2	4.8±0.4	0.45
LH/FSH ratio	2.5±0.5	2.0±0.6	0.03
AMH, ng/mL	13.3±1.4	11.9±0.9	0.04
HOMA-IR	2.5±1.4	2.1±0.7	0.05

Table 5. Comparison of Mean Outcomes Measures Between the 2 Groups After 12 Weeks of Intervention

Variables	Mean ± SD Outcomes Measures		*P* Value
	Study Group (n=11)	Control Group (n=10)	
BMI (kg/m²)	25.6±0.1	25.0±1.2	0.51
FF, ng/dL	1.09±0.1	1.5±0.05	0.01
TT, ng/dL	60.0±0.1	63.0±1.9	0.05
LH, mIU/mL	6.9±0.9	9.9±0.2	0.02
FSH, mIU/mL	4.8±0.6	4.8±0.4	0.67
LH/FSH ratio	1.3±0.0	2.0±0.6	0.03
AMH, ng/mL	8.5±1.3	11.9±0.9	0.01
HOMA-IR	1.9±1.5	2.1±0.7	0.04

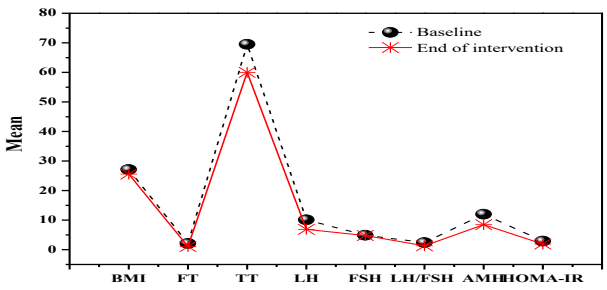

Figure 2. Outcomes Measures Within the Study Group.

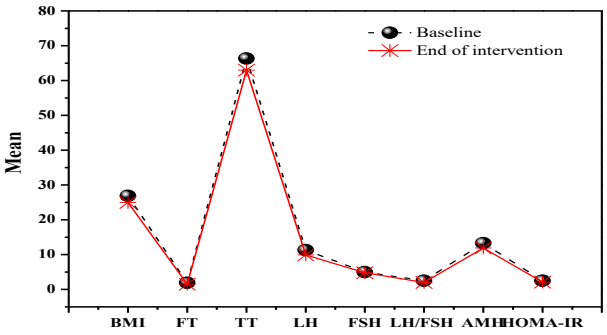

Figure 3. Outcomes Measures Within the Control Group.

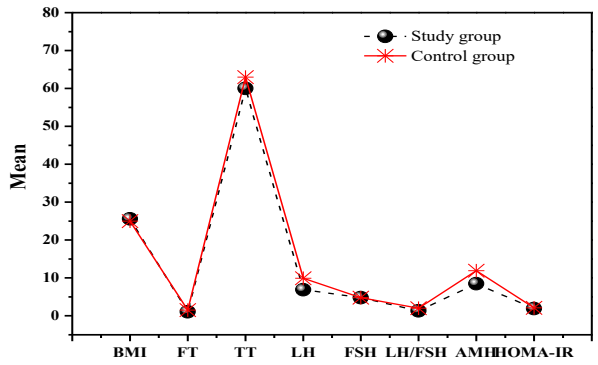

Figure 4. Comparison of Mean Outcomes Measures Between the 2 Groups at the End of Intervention.

A significant decrease of total and free testosterone levels after dietetic-induced weight reduction was affirmed and agreed with our study. Additionally, controlled trials have obtained similar outcomes, despite the fact that others did not report any impact. Weight reduction can be followed by a significant improvement in SHBG concentration, which is steady with a diminishment of the free androgen.[28,30]

In spite of the fact that exercise in overweight or obese PCOS women enhances insulin sensitivity, the impact of exercise is by all accounts through mechanisms inconsequential to weight reduction[31]; exercise can improve rates of glucose clearance and the skeletal muscle sensitivity take-up to insulin.[32]

In the present study, diminished HOMA, IR is an indication of progress in insulin sensitivity and decreased IR.

Chronic anovulation is a common characteristic of PCOS women, and the return of ordinary ovulatory function represents the main target to be accomplished for PCOS women complaining of ovarian dysfunction and/or infertility.

In our study, the menstrual pattern was as follows: 6 of 9 reported 3 regular menses in the study group, with 5 of 7 reported 3 regular menses in the control group.

The mechanisms responsible for the beneficial outcome of weight reduction on menses changes and fertility likely rely upon the parallel reduction of both hyperinsulinemia

and hyperandrogenemia. Evidence exists that dietetic-initiated weight reduction may enhance both menstrual variations from the norm and spontaneous ovulation in the larger part of PCOS women.[33] Unexpectedly, it ought to be noted that obtainable information on the results of weight reduction on menses variations from the norm among obese PCOS women have frequently been obtained in uncontrolled trials, in studies including a control group who neglected to complete the study protocol, and even with insignificant (5% of baseline) weight reduction throughout treatment.[34]

Our data suggest improved outcomes for PCOS women treated with laser acupoints (SG) compared with those treated with placebo laser acupoints (CG). The mechanism, by which laser influences the insulin sensitivity, is still unknown. Notwithstanding, there are numerous physiological proposals that may clarify the change in insulin sensitivity.[35] It has also been found that women with PCOS have low-grade inflammation, which might be a reason for IR.

Use of laser reduces the level of cytokines discharged from white blood cells (inflammatory response)[36]; cytokines such as TNF-alpha, IL-1 beta, and IL-8 proteins contribute to IR and atherosclerosis.[37]

Utilization of laser stimulates the respiratory electron transport chain, resulting in (1) changes in the reduction/oxidation status of the mitochondria which leads to enhanced ATP synthesis (Krebs cycle), (2) activation of sodium/potassium pump modifies cell membrane permeability to the flow of calcium.[38]

The enhancement of ions transportation over the cell membrane, that occur in instances of hyperinsulinemia or IR, may enhance the insulin action on the cells and contribute to lessening the insulin level.[39]

These acupoints compare to particular regions on the body surface, which exhibit high electrical conductance on account of the existence of high density of gap junctions alongside cell margins. They go about as convergent points for electromagnetic fields. A high metabolic rate, high temperature, and calcium ion concentration are likewise seen at these points.[40]

Laser is a type of electromagnetic radiation used to stimulate acupuncture points using the same principles of point determination as for needle acupuncture.

An explanation for the changes for PCOS women in the SG compared with those in the CG is that laser acupoint placed in the identical innervation part as the ovary reduces sympathetic activity that prompts diminished discharge of ovarian androgens. In parallel, the action of higher centers is modulated by the discharge of opioids, specifically B-endorphin which thusly influence GnRH secretion and the menstrual cycle. Animal studies have exposed that acupuncture therapy standardized GnRH emission and influenced peripheral GnRH levels.[41] In women with PCOS, there is an increased sympathetic nerve activity and an increased B-endorphin secretion. Laser acupoint diminishes central B-endorphin, causing a decreased sympathetic tone, decreased LH and release of B-endorphin into the circulation system. Different investigators have exposed that, acupuncture likewise affected serum levels of LH, FSH, E2, and P in typically ovulatory or anovulatory women.[42] Another study by Stener-Victorin et al[14] assessed the impact of electroacupuncture (EA) for induction of ovulation on 24 PCOS women. The proportion of menstrual cycles in all participants appeared to be enhanced by 15%-66% up to 3 months post-treatment. The BMI, waist/hip circumference ratio, LH/FSH ratio, serum testosterone concentrations and the B-endorphin concentration diminished significantly after treatment, showing that acupuncture could be considered as an option or subordinate to pharmacological induction of ovulation. Through its central sympathetic-inhibitory impact, acupuncture may diminish uterine artery resistance and in this way, improve uterine blood flow.[43] The peripheral influence of acupuncture in enhancing uterine blood flow and hereafter endometrial thickness also gives encouraging information in regards to its potential positive effect on implantation and enhancement of infertility treatment outcomes. As of late, skin light contact has appeared to stimulate mechanoreceptors with slow conducting unmyelinated (C) afferents which regulate activity in the central nervous system[44] of both groups in our study.

Limitations of our study were changes in the factors: psycho-physiological, social and cultural level of PCOS participants, which may or may not have had an impact on the outcomes, but until now have not been clarified in the literature. Future scientific studies on the effectiveness of various physical therapy modalities as ultrasonic acupoints in the treatment of PCOS women is really advised.

Conclusion

Based on the present analysis, laser acupoints stand for an efficient and safe form of acupuncture for the treatment of PCOS women and could be considered as a viable alternative or complement to pharmacological induction of ovulation.

Conflict of Interests

The authors declare that they have no competing interests.

Ethical Considerations

The proposal of this study was approved by the research ethics committee, Faculty of Physical therapy, Cairo University (No: P.T. REC/012/001534) and by the Local Review Board of Kafrelsheikh General Hospital.

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